

nucleotides are the inverted terminal repeat (ITR) (nucleotides 1-103), poly-adenylation signal (nucleotides 116-261), a human E2F-1 promoter (nucleotides 283-555), E1A gene (nucleotides 574-1647) and a portion of the E1b gene (nucleotides 1648-1802) are indicated (SEQ ID NO:3). Figure 3C: Regions in the last 531 nucleotides are the PacI restriction site (nucleotides 33967-33974) (underlined), the packaging signal (nucleotides 34020-34217 and the ITR (34310-34412). --

**Page 2, description of Figure 4:**

-- Figure 4: Sequence of Ar6F from left end of viral DNA (SEQ ID NO:5). The first 660 nucleotides at the left end of Ar6F. The ITR (nucleotides 1-103), a multiple cloning site (MCS) (nucleotides 104-134) and a portion of the E1A gene (nucleotides 135-660) are shown. --

**Page 2, description of Figure 5:**

-- Figure 5: Sequence of Ar6pAF from left end of viral DNA (SEQ ID NO:6). The first 660 nucleotides at the left end of Ar6pAF. The ITR (nucleotides 1-103), the SV40 early polyA signal (nucleotides 104-134) and a portion of the E1A gene (nucleotides 298-660) are shown. --

**Page 3, description of Figure 10:**

-- Figure 10: Survival of tumor-bearing animals after intratumoral injections of vectors to H460 tumors. Survival of tumor bearing animals after treatment with Ar6pAE2fF. Animals were observed until study day 32. Numbers of animals in each treatment group were as follows: HBSS, n = 13; Ar6pAE2fF at  $5 \times 10^8$ , n = 13;  $5 \times 10^9$ , n = 13; and  $5 \times 10^{10}$  particles/dose/day, n=12; and Addl327 at  $5 \times 10^{10}$  particles/dose/day, n =12. The survival of animals was analyzed by the Mantel-Haenszel logrank test. --

**Page 3, description of Figure 12:**

-- Figure 12: Survival of tumor-bearing animals after intratumoral injections of vector to Hep3B tumors. Survival of tumor bearing animals after treatment with Ar6pAE2fF. Animals were observed until study day 32. Numbers of animals in each treatment group were

as follows: HBSS, n = 11; Ar6pAE2fF at  $5 \times 10^8$ , n = 11;  $5 \times 10^9$ , n = 11; and  $5 \times 10^{10}$  particles/dose/day, n=10; and Add1327 at  $5 \times 10^{10}$  particles/dose/day, n=11. The survival of animals was analyzed by the Mantel-Haenszel logrank test. --

**Page 5, description of Figure 25:**

-- Figure 25: Schematic diagram of PCR and overlap PCR for  $\Delta$ gp19 donor plasmids

The mGM-CSF or hGM-CSF cDNA was inserted into the E3 region replacing the E3-gp19 open reading frame (ORF) using two steps of PCR amplification. In the first step, 3 individual PCR amplifications were carried out using 3 pairs of primers and corresponding DNA templates. In the second step, the 3 DNA fragments generated in first step were mixed as the template DNA for the overlap PCR amplification using primer 1 and primer 6 as primers. The overlap PCR product was then digested with BsiWI/NotI and used to replace the BsiWI/NotI region of adenoviral E3 containing the E3-gp19 open reading frame. --

**Page 5, description of Figure 26:**

-- Figures 26A-26B: Schematic Diagram of Δgp19 Vectors. Figure 26A: Sequence of native E3 region (SEQ ID NO:9 and SEQ ID NO:13). Figure 26B: Sequence Comparison of Δgp19 vectors at the junction between E3-6.7 and GMCSF (SEQ ID NO:98; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13). --

**Page 10, description of Figure 49:**

-- Figure 49: E4 expression is dependent on the hTERT promoter. Adenoviral E4 expression measured by semi-quantitative RT-PCR. The E4 region is encoded on the opposite strand in the viral genome. Total RNA was isolated from Hep3B cells 24 hours after infection with 10 ppc of Ar17pAE2fTtex. Depicted is a schematic diagram of the right end of the Ar17pAE2fTtex viral genome with relative positions of primers used in RT-PCR reactions along with the approximate size of the products. PCR 2.f paired with PCR 3.r or PCR 4.r were designed to detect all E4 transcripts. PCR 2.f paired with PCR 5.r was used to detect transcripts that initiated from any cryptic start sites upstream of the E4 region. +1, indicates the approximate position of transcriptional initiation site of the native hTERT promoter. --

**Page 10, description of Figure 51:**

a9 -- Figure 51: Efficacy of Ar17pAE2fTrtex in Hep3B model. Tumors were established by injecting  $1 \times 10^7$  Hep3B cells subcutaneously into the right flank of 6-8 week old female nude mice (Harlan). Two weeks after implantation, mice with tumors ranging from  $91.6 - 218.5 \text{ mm}^3$  were selected and randomly distributed into groups (n=17-18). Each mouse was weighed prior to intravenous injection. The control groups received HBSS or Addl312 at  $4.5 \times 10^{12} \text{ vp/kg}$  (n=18). Ar17pAE2fTrtex treatment groups received  $1.5 \times 10^{12}$  (n=18),  $3.0 \times 10^{12}$  (n=17), or  $4.5 \times 10^{12}$  (n=18) vp/kg. All dose volumes were 10 ml/kg. Groups means + SEM are represented. \*,  $p < 0.05$  vs. HBSS controls (Dunnett test). --

**Page 11, description of Figure 53:**

a10 -- Figure 53: Body weight changes. Group mean body weights are shown following a single intravenous injection of the indicated test article. The number of animals evaluated at each scheduled data collection time point was 18-33, except for SD29 when n = 9-22. Vector doses were adjusted on the basis of individual animal body weight on the day of dosing. Lo Dose:  $1.5 \times 10^{12} \text{ vp/kg}$ ; Mid Dose:  $3.0 \times 10^{12} \text{ vp/kg}$ ; Hi Dose:  $4.5 \times 10^{12} \text{ vp/kg}$ . Group means + SD are represented, with no statistically significant differences between groups. --

**Page 11, description of Figure 54:**

a11 -- Figure 54: Efficacy of Ar17pAE2fTrtex in Hep3B model. Comparison of *in vivo* growth of Hep3B tumors after a single iv injection of Ar17pAE2fTrtex at  $3 \times 10^{12}$  (n=16) or  $4.5 \times 10^{12}$  (n=16) particles/kg. Control groups were injected with HBSS (n=16) or Addl312 (n=16) at  $4.5 \times 10^{12}$  particles/kg. Data is expressed as mean tumor volume + SE. (\* $p < 0.05$ ) For both Ar17pAE2fTrtex treated groups compared to HBSS treated controls using one-way ANOVA with Student-Newman-Keuls test for multiple comparison. --

**Pages 11-12, description of Figure 57:**

a12 -- Figure 57: Dose-dependent anti-tumor efficacy. Tumors were established by injecting  $1 \times 10^7$  Hep3B cells subcutaneously into the right flank of 6-8 week old female nude mice (Harlan). Two weeks after implantation, mice with tumors ranging from  $90 - 215 \text{ mm}^3$  were selected and randomly distributed into groups (n=12/group). Each mouse was

weighed prior to intravenous injection. The control mice received HBSS. Ar17pAE2fFTrtex treatment groups received  $3 \times 10^{11}$  (n=12),  $6 \times 10^{11}$  (n=12),  $1 \times 10^{12}$  (n=12), or  $3 \times 10^{12}$  (n=12) vp/kg. All dose volumes were 10 ml/kg. Groups means (+SEM) are represented. \*, p < 0.05 vs. HBSS controls (Dunnett's method). --

**Page 12, description of Figure 58:**

-- Figure 58: Individual tumor volumes following intravenous administration of Ar17pAE2fFTrtex for study days 3 through 22 are presented. All dose volumes were 10 ml/kg. A) The control group treated with HBSS. Treatment groups received Ar17pAE2fFTrtex at B)  $3 \times 10^{11}$  vp/kg, C)  $6 \times 10^{11}$  vp/kg, D)  $1 \times 10^{12}$ , or E)  $3 \times 10^{12}$  vp/kg. (n=12 / group). --

**Page 12, description of Figure 62:**

-- Figure 62: Effect on body weight in SCID mice. The mean body weight change as a percent of the SD1 body weight +st dev was followed for a cohort of five mice in each treatment group. Animals were injected with a single intravenous dose of the indicated vectors on SD1. \*, p < 0.05 vs. HBSS (one-way ANOVA). --

**Page 37, last 3 lines:**

-- Hexon Forward primer: 5'-CTTCGATGATGCCGAGTG-3' (SEQ ID NO:95)  
Hexon Reverse primer: 3'-GGGCTCAGGTACTCCGAGG-3' (SEQ ID NO:96)  
Hexon Probe: 5'-FAM-TTACATGCACATCTCGGGCCAGGAC-TAMRA-3' (SEQ ID NO:97) --

**REMARKS**

In response to the Notice to File Missing Parts, Applicants have provided an initial paper copy of the sequence listing, an initial computer readable form (CRF) copy of the sequence listing, as well as an amendment directing its entry into the specification. Pursuant to 37 CFR §§ 1.821-1.825, the undersigned states that the Paper Copy and the Computer Readable Form are identical and contain no new matter.